

# Preparation of n-Butyl 4,5-Epoxy pentanoate and Opening Reaction of Its Epoxide Ring

by Tadashi Ishikawa\* & Hisao Hidaka\*\*

## Summary

n-Butyl 4,5-epoxypentanoate was prepared by the epoxidation of n-butyl 4-pentenoate with 40% peracetic acid and the appropriate reaction conditions such as solvent effect, addition of sodium acetate as a stabilizer, reaction temperature, and time have been investigated. Moreover, several ring reactions of the epoxide with various nucleophilic reagents have been also studied.

## Introduction

Though the epoxidation of double bond has been extensively reported(1~6), there is no paper on the ester of  $\omega$ -unsaturated carboxylic acid. Depending upon the peracids employed and the operating conditions, either an epoxide or  $\alpha$ -glycol may be obtained. n-Butyl 4-pentenoate **1** reacted with 30%  $\text{H}_2\text{O}_2$ -acetic acid to give 5-hydroxy-4-pentanolide and 5-acetoxy-4-pentanolide as reported in our previous paper (7), but attempts to isolate n-butyl 4,5-epoxypentanoate **2**, which was assumed to be the intermediate were unsuccessful. It was necessary to employ a peracid and select appropriate reaction conditions for the preparation of **2** in this manner. As far as we know **2** is a new compound, of which the characterization was done by elemental analysis, molecular weight determination, and by ir and pmr spectra.

Furthermore, the cleavage reactions of **2** with nucleophilic reagents such as acetic acid, dimethyl sulfoxide, ethylene glycol, phenyl isocyanate, etc. were investigated.

## Experimental

### *Spectra and analysis*

The spectra were obtained as follows: pmr with Varian Associates A-60 spectrometer in  $\text{CCl}_4$  solution using TMS as the internal standard; ir with Hitachi EPI-2 and Perkin-Elmer 337 Grating spectrometers; mass spectra with a Varian Associates CH-7 instrument. Molecular weight was measured with Mechrolab Vapour Pressure Osmometer 301-A in methyl ethyl ketone solvent. The elemental analysis was performed with a Shimadzu UM-3B analyzer.

### *Materials and preparation*

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\* 理工学部化学科教授 物理化学

\*\* 理工学部化学科助教授 物理化学

*n*-Butyl 4-pentenoate 1

1 (Towa Gosei Chemical Co.) was purified by vacuum distillation three times using hydroquinone as an antioxidant and checked by gc; bp 50°C/5mmHg;  $n_D^{20}$  1.4259,  $D_4^{20}$  0.8865. Peracetic acid solution containing 40% peracetic acid and 4.68%  $H_2O_2$  in acetic acid (Mitsubishi-Edogawa Chemical Co.), boron trifluoride etherate (Tokyo Kasei Co.) and other materials were of analytical reagent grade and were used without further purification.

*n*-Butyl 4,5-epoxypentanoate 2

In a three-necked, round bottomed flask were placed 19.5 g (0.124 mol) of 1 and 4 g (0.048 mol) of sodium acetate in 300 ml of chloroform, 35 g (0.19 mol) of 4% preacetic acid being added dropwise during the course of 0.5 hr at 30°C. After the exothermic reaction, it was moreover allowed to stir for 2.5 hr at 30°C. The mixture was poured into 200 ml of water and extracted several times with ether. The ether layer was washed with aqueous sodium carbonate and then with water, dried over anhydrous sodium sulfate, and the ether was evaporated to give 10.3 g (59.3 %) of 2 by vacuum distillation, bp 70~75°C/0.5 mmHg; ir  $\nu_{max}$  (Nujol) 3050, 2962, 1770(C=O, ester), 1250 ( $\alpha$ -epoxy), 1165, 820, 750  $cm^{-1}$ ; pmr ( $\delta$ ) 0.95(3H, t,  $-CH_3$ ), 2.33(2H,  $-CH_2-COO-$ ), 2.42(1H,  $\overset{H}{\underset{\curvearrowright}{C}}-\overset{\curvearrowright}{C}-$ ), 2.72 (1H,  $\overset{H}{\underset{\curvearrowright}{C}}-\overset{\curvearrowright}{C}-$ ), 2.98 (1H,  $\overset{H}{\underset{\curvearrowright}{C}}-\overset{\curvearrowright}{C}-$ ), 3.95 (2H, t,  $-COOCH_2-$ );

Mass spectrum; parent ion  $m/e$  172, prominent peaks at  $m/e$  99, 71, 57, 43. Anal. Calcd. for  $C_9H_{16}O_3$ : C, 62.78; H, 9.30. Found: C, 62.50; H, 9.25.

## 5-hydroxy-4-pentanolide 3 and 5-acetoxy-4-pentanolide 4

3 and 4 were prepared by heating 13 g (0.07 mol) of 2 and 20 g (0.33 mol) of acetic acid with stirring for 6 hr at 70°C. After drying over anhydrous sodium sulfate, acetic acid was evaporated under reduced pressure. The mixture of 3 and 4 was distilled at bp 115-132°C/7mmHg and was not separated.

The above mixture was saponified with 10% aqueous alkali solution for 12 hr to give the pure 3 by distillation. bp 125°C/2mmHg;  $n_D^{20}$  1.4650; ir  $\nu_{max}$  (Nujol) 3420 ( $-OH$ ), 1780  $cm^{-1}$  (C=O,  $\gamma$ -lactone); pmr ( $\delta$ ) 2.30 (2H, m,  $\beta$ -methylene), 2.45 2.40 (2H,  $-CH_2-COO-$ ), 3.72 (1H, s,  $-OH$ ), 4.33(2H, d,  $-O-CH_2-C-$ ), 4.62 (1H, m,  $-CH-$ ). Mol. Wt. Calcd. 116, Found 118. Anal. Calcd. for  $C_5H_8O_3$ : C, 51.72; H, 6.94. Found: C, 51.36; H, 6.99.

On the other hand, the pure 4 was obtained by the acetylation. The above mixture was reacted with acetic anhydride in the presence of sodium acetate as a catalyst. After heating under reflux at 140°C for 2 days, acetic anhydride was evaporated and 4 was distilled under reduced pressure. bp 114°C/3mmHg.  $n_D^{20}$  1.4553; ir  $\nu_{max}$  (Nujol) 1780 (C=O,  $\gamma$ -lactone), 1740  $cm^{-1}$  ( $-O-CO-CH_3$ ); pmr ( $\delta$ ) 4.62 (1H, m,  $-CH-$ ), 4.07-4.18 (2H, d,  $-COO-CH_2-$ ), 2.45-2.40 (2H,  $\alpha$ -methylene), 2.30 (2H,  $\beta$ -methylene), 2.05(3H, s,  $-O-CO-CH_3$ ); Mol. Wt. Calcd. 158, Found 159. Anal. Calcd. for  $C_7H_{10}O_4$ : C, 53.15; H, 6.39. Found: C, 52.81; H, 6.25.

*n*-Butyl 4,5-dihydroxypentanoate 5

In 350 ml of dioxane, were placed 17 g (0.1 mol) of **2** and 100 g of 1% sulfuric acid solution and the mixture was heated with stirring for 6 hr at 80°C. After the solvent and water were removed, the residue was extracted with ether, dried, and distilled to afford 3 g (15.8%) of **5**, bp 65~70°C/4.5mmHg; ir  $\nu_{\text{max}}$  3450 (broad str., -OH), 1770  $\text{cm}^{-1}$  (str., ester); pmr ( $\delta$ ) 3.95 (2H, t, -COOCH<sub>2</sub>-), 3.72-3.69 (2H, two singles, -OH), 2.33 (2H, -CH<sub>2</sub>COO-), 0.95 (3H, t, -CH<sub>3</sub>-CH<sub>3</sub>); Anal. Calcd. for C<sub>9</sub>H<sub>18</sub>O<sub>4</sub>: C, 56.84; H, 9.47. Found: C, 56.78; H, 9.40.

*n*-Butyl-5-hydroxy-4-oxopentanoate **6**

The solution of 17.2 g (0.1 mol) of **2** and 0.2 ml of boron trifluoride etherate in 40 ml of dimethyl sulfoxide was heated on a steam bath for 22 hr. The reaction mixture was poured into ice water and extracted with chloroform several times. Distillation gave 11.0 g (58.5%) of **6**, mp 91~95°C/2mmHg; ir  $\nu_{\text{max}}$  3450 (med., -OH), 1770 (str., ester), 1720 (str.,  $\gamma$ -ketone), 1250  $\text{cm}^{-1}$  (str.); pmr ( $\delta$ ) 4.10 (2H, t, -COOCH<sub>2</sub>), 3.80 (2H, s, -O-CH<sub>2</sub>-CO-), 3.65 (1H, s, -OH), 0.93 (3H, s, -CH<sub>3</sub>); Anal. Calcd. for C<sub>9</sub>H<sub>16</sub>O<sub>4</sub>: C, 57.46; H, 8.51. Found: 57.49; H, 8.50.

5-(2-Hydroxyethoxy)-4-pentanolide **7**

In a 500 ml round bottomed flask, 17.2 g (0.1 mol) of **2** was treated with 23 ml (0.8 mol) of ethylene glycol in the presence of 7% boron trifluoride etherate. The reaction mixture was stirred at 60°C for 6 hr in a water bath. After the unchanged ethylene glycol was taken off, a colorless liquid was distilled under reduced pressure; yield 5 g (31%); bp 134~136°C/4mmHg; ir 3400 (-OH), 1780 (C=O,  $\gamma$ -lactone), 1070  $\text{cm}^{-1}$  (C-O-C); pmr ( $\delta$ ) 4.62 (1H, m, -C-CH-C-), 4.48 (2H, d, -O-CH<sub>2</sub>-C-), 3.80-3.90 (4H, two triplets, -OCH<sub>2</sub>CH<sub>2</sub>O-), 2.65 (1H, s, OH), 2.65 (1H, s, -OH), 2.40 (2H, -CH<sub>2</sub>-COO-): Anal. Calcd. for C<sub>7</sub>H<sub>12</sub>O<sub>4</sub>: C, 52.49; H, 7.55. Found: C, 52.80; H, 7.51.

5-(2-butoxycarbonylethyl)-3-phenyl-2-oxazolidone **8**

i) *Tetraethylammonium bromide (TEAB) catalized opening of the epoxide ring.*

In an autoclave was placed the mixture of 25.8 g (0.15 mol) of **2** and 15.4 g (0.13 mol) of phenyl isocyanate in 50 ml of dioxane in the presence of 0.46 g of TEAB and heated to 200°C for 4 hr under the pressure of about 12 atm. After cooling, the dioxane was then removed. The residue was washed with water and extracted with chloroform.

After the evaporation of the dried extract, recrystallization from ethanol gave white leaflets; mp 36~37°C; yield 8.3 g (21.9%); ir, 2990, 1775 (str., C=O, oxazolidone), 1735 (str., C=O, butoxycarbonyl), 1610, 1480, 1410  $\text{cm}^{-1}$ ; pmr ( $\delta$ ) 7.45 (5H, -C<sub>6</sub>H<sub>5</sub>), 4.65 (1H, m, -C-CH-C-), 4.10 (2H, t, -COOCH<sub>2</sub>-), 3.83 (2H, s, -N-CH<sub>2</sub>-C-), 0.95 (3H, t, -CH<sub>3</sub>); Anal. Calcd. for C<sub>16</sub>H<sub>21</sub>NO<sub>4</sub>: C, 65.95; H, 7.22; N, 4.81. Found: C, 65.95; H, 7.20; N, 4.79.

ii) *Lithium chloride catalized opening of the epoxide ring.*

In a 300 ml three-necked flask were placed 34.4 g (0.2 mol) of **2** and 23.8g

(0.2 mol) of phenyl isocyanate in the presence of 82 mg (2 m mol) of lithium chloride. The temperature was kept approximately 190°C with stirring for 15 hr. The mixture was cooled, poured into water, and extracted with ether to afford 4.2g(10.2 %) of white crystals. Recrystallization from ethanol gave pure 8, mp 35~36°C.

The elemental analysis, ir, and pmr of this compound were identical with those of the sample prepared by the catalyst of TEAB.

## Results and Discussion

### *Synthesis of n-butyl 4,5-epoxypentanoate*

When 1 was reacted with 30% hydrogen peroxide in acetic acid, the epoxide 2 could not be obtained and the reaction immediately proceeded to the lactonized compounds 3 and 4. When 40% peracetic acid as an oxidizing agent was successfully prepared in good yield.

The characterization and identification was performed by ir, pmr and elemental analysis as mentioned on experimental. The mass spectrum of 2 showed characteristic fragments of  $\text{CH}_2\text{-CH}^+$  (m/e, 43),  $\text{C}_4\text{H}_9^+$  (57),  $\text{CH}_2\text{-CH-CH}_2\text{CH}_2^+$  (71), and  $\text{CH}_2\text{-CH-CH}_2\text{CH}_2\text{CO}^+$  (99).

The parent peak was m/e 172 and the following isotopic composition : P+1, 10.10 % ; P+2, 1.06% gave the molecular formula  $\text{C}_9\text{H}_{16}\text{O}_3$ .

In order to isolate 2, it was necessary to select appropriate operating conditions. The effects of solvent, catalyst, temperature and time were investigated as following.

#### i) Solvent effect

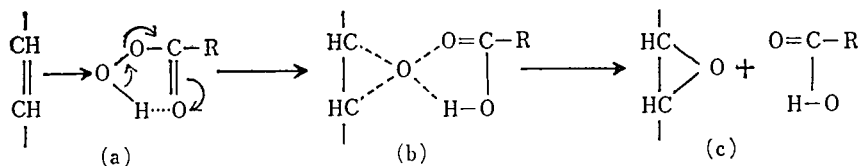
To research this effect, various solvents were employed under the same reaction condition at 40°C for 6 hr. These results were summarized in Table I.

Table I. Effect of solvent on the epoxidation\*

Solvent	Yield (%)	Solvent	Yield (%)
Carbon tetrachloride	37.2	Ethyl ether	24.0
Benzene	37.2	Acetic acid	22.1
n-Hexane	29.5	Acetone	18.0
n-Pentane	23.1	Dimethyl formamide	14.0
Chloroform	31.0	Dioxane	14.0

\* 1 : 39.0g (0.25 mol), 40%  $\text{CH}_3\text{COOOH}$  : 48.0g (0.25 mol)  
 $\text{CH}_3\text{COONa}$  : 4.0 g, reaction temperature : 40°C, time : 3 hr

2 was comparatively obtained in higher yield in nonpolar solvents such as carbon tetrachloride, benzene, and n-hexane rather than in polar solvents such as acetone, dioxane, and dimethyl formamide. Gould has reported that the transition state (a) of epoxidation would have the same mechanism as the so-called  $\pi$ -complex of the addition reaction (8).



The formation of  $\pi$ -complex appeared not to be hindered in the nonpolar solvent, whereas the approach of the double bond to a peracid in the polar solvent seemed to interfere owing to the intermolecular hydrogen bonding.

In case of acetone, white needles (mp 73°C) were obtained besides the preparation of **2**. It was identified to be the peroxide of acetone by ir  $\nu_{\max}$  880, 840  $\text{cm}^{-1}$  (str. C-O-O-C) and pmr ( $\delta$ ) 1.38 (s.  $-\text{CH}_3$ ). Murai and so on (9, 10) have published that acetone reacted with hydrogen peroxide to give  $(\text{CH}_3)_2\text{C}(\text{OOH})_2$ , its peroxy dimer or its cyclic peroxy trimer. The similar reaction was thought to occur between acetone and peracetic acid.

#### ii) Influence of sodium acetate

The yield of **2** increased with a quantity of sodium acetate up to 0.048 mol, whereas decreased above this quantity. The optimum amount was 0.048 mol as shown in Table II.

Table II. Effect of stabilizer\*

$\text{CH}_3\text{COONa}$ (mol)	Yield (%)
0	15.5
2 (0.024)	37.9
4 (0.048)	59.3
8 (0.096)	34.5
16 (0.192)	24.1

\* **1** : 19.5g (0.125 mol), 40%  $\text{CH}_3\text{COOOH}$  : 36.0g (0.19 mol)  
chloroform : 150 ml, reaction temperature : 30°C, time : 3 hr

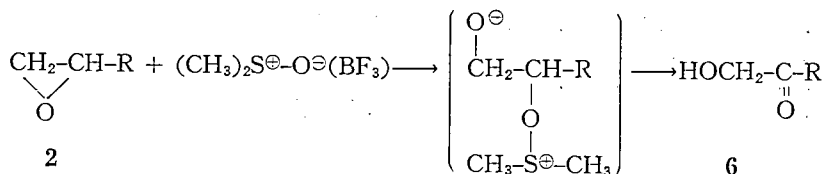
It has been reported by Payne (11) that the epoxidation depended on the pH. As the pH become higher, the activation of peracid would tend to be lowered. Sodium acetate would play the role of buffer in this reaction. As the quantity of sodium acetate was larger, the unchanged **1** was considerably remained. While, in the absence of sodium acetate, the opening of the epoxide by acetic acid containing peracetic acid proceeded to give either a glycol or its monoester.

#### iii) Influence of reaction temperature and time

The effects of temperature and time on the epoxidation were investigated in the presence of sodium acetate as summarized in Table III.

The yield of **2** increased with raising of reaction temperature from 0°C to 30°C to reach almost about 60% at the temperature above 30°C. With respect to reaction time, the yield was higher up to 60%~70% according as the time was longer than 3 hr.

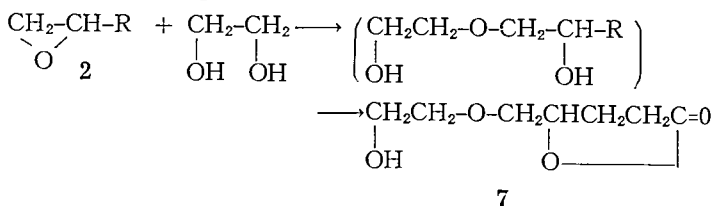




This reaction have the same mechanism reported by Cohen(12) on the oxidation of 1,2-epoxycyclohexane with boron trifluoride to give 2-hydroxycyclohexanone.

iv) *Reaction of 2 with ethylene glycol*

The reaction of 2 with ethylene glycol in the presence of trifluoride gave mainly 5-(2-hydroxyethoxy)-4-pentanolid 7.



The dihydroxy derivative could not be obtained as an intermediate because of lactonization with ease.

v) *Reaction of 2 with phenyl isocyanate*

Quaternary ammonium halide have been known to be an efficient catalyst for the addition of isocyanate with epoxide (13, 14). The reaction of 2 with phenyl isocyanate in the presence of TEAB was carried out under the autogenous pressure. The substituted oxazolidone 8 was prepared in poor yield. This formation was thought to be the similar mechanism as Gulbins' report (15). Lithium chloride was also used instead of TEAB as a catalyst but the yield of 8 was lower than in the presence of TEAB.

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